

# Optimized multielectrode tDCS modulates corticolimbic networks

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Transcranial direct current stimulation (tDCS) is a noninvasive neuromodulatory technique using weak electrical currents to alter cortical excitability. Currently, studies are exploring distinct stimulation parameters to optimize tDCS effects. Here, we aimed to test the differential effect of a novel, computationally-optimized multielectrode montage designed to improve targeting and efficiency of the induced electric field.

## Methods

In a randomized, single-blind sham-controlled crossover study, 20 healthy subjects underwent three tDCS sessions (conventional, multielectrode and sham) using the Starstim system with 25 cm<sup>2</sup> sponges and eight 3 cm<sup>2</sup> Ag/AgCl Pi electrodes respectively, with two weeks of inter-session interval. Stimulation was applied for 20min targeting prefrontal regions. Resting state (rs) fMRI scans were acquired immediately after tDCS sessions in order to identify functional tDCS-induced changes. We firstly examined the fractional amplitude of low-frequency fluctuations (fALFF) to determine between-condition differences on regional brain activity. Then, areas exhibiting fALFF differences were selected as regions-of-interest in a seed-based functional connectivity (FC) analysis within areas of the corticolimbic network. fALFF and Connectivity analyses were conducted using REST software in SPM8. In both analyses, statistical significance was estimated using a combination of voxel- and cluster-level thresholds. The cluster extent threshold for each analysis was determined using the AlphaSim function implemented in the SPM-REST toolbox to provide values equivalent to a FWE correction of  $p < 0.05$ .

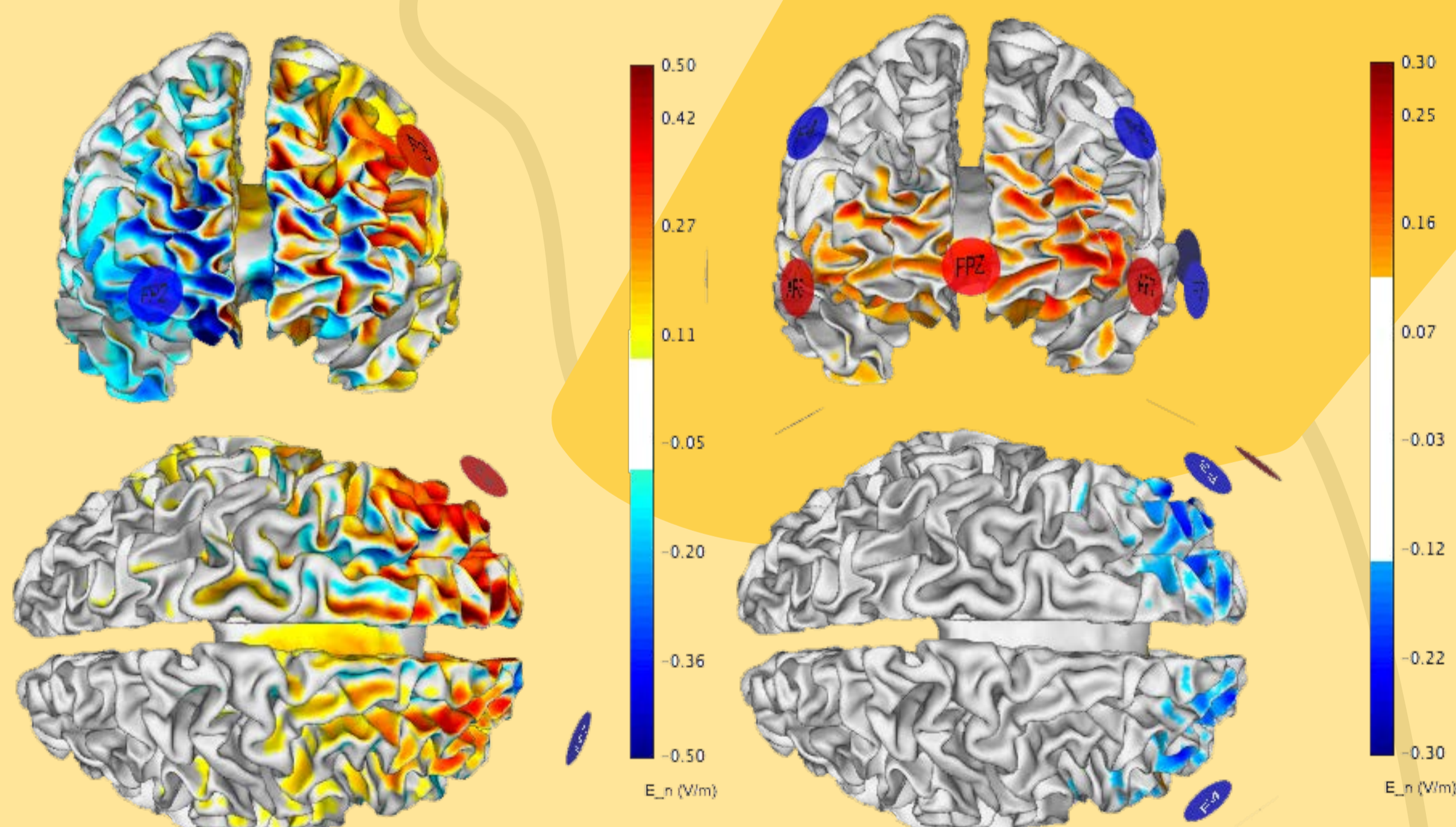


Figure 1: Conventional (left) and multielectrode (right) montages..

## Results

The multielectrode montage resulted in significantly higher fALFF values in frontopolar, middle and superior prefrontal cortices (Figure 2).

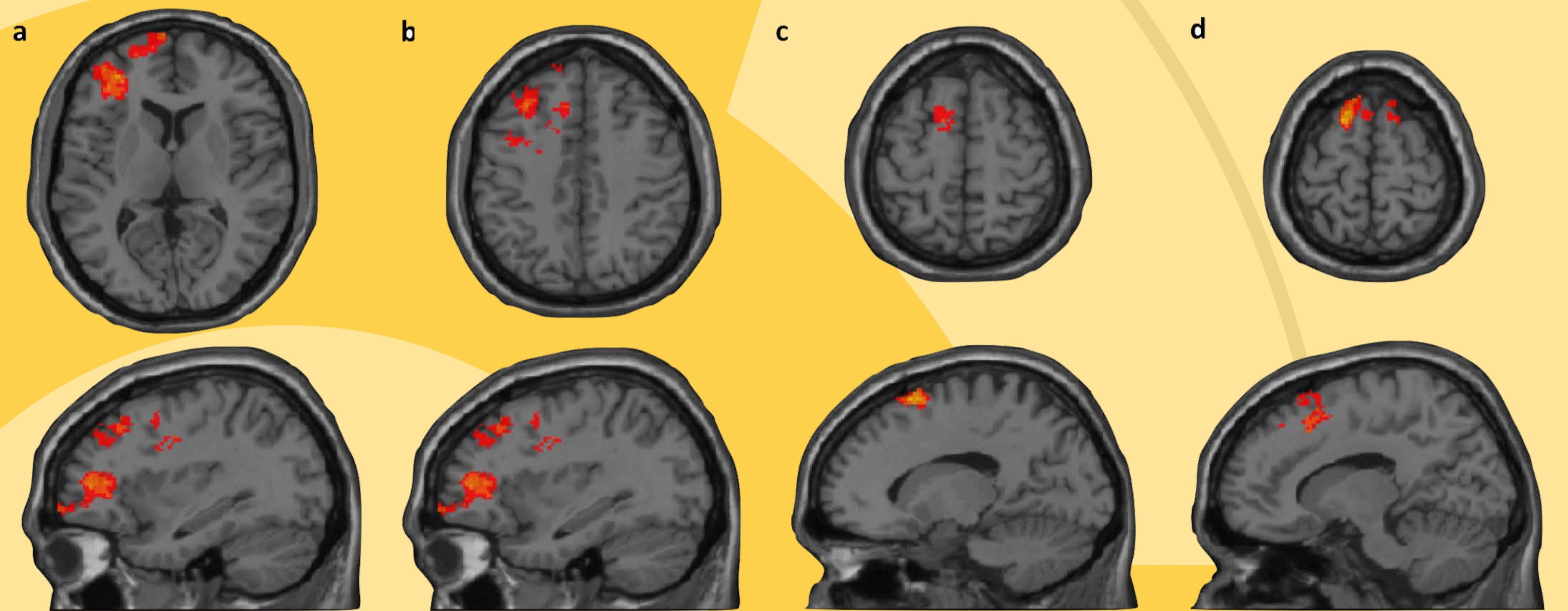


Figure 2: Increment of fALFF in multielectrode montage versus sham in: a) left frontal pole b) left middle frontal gyrus c) left superior frontal gyrus and d) bilateral frontal gyrus. Top row axial plane and bottom row sagittal plane. Alphasim corrected,  $p < 0.01$ .

Furthermore, an increase in FC between these regions and limbic regions was specifically observed in this condition (Figures 3 and 4).

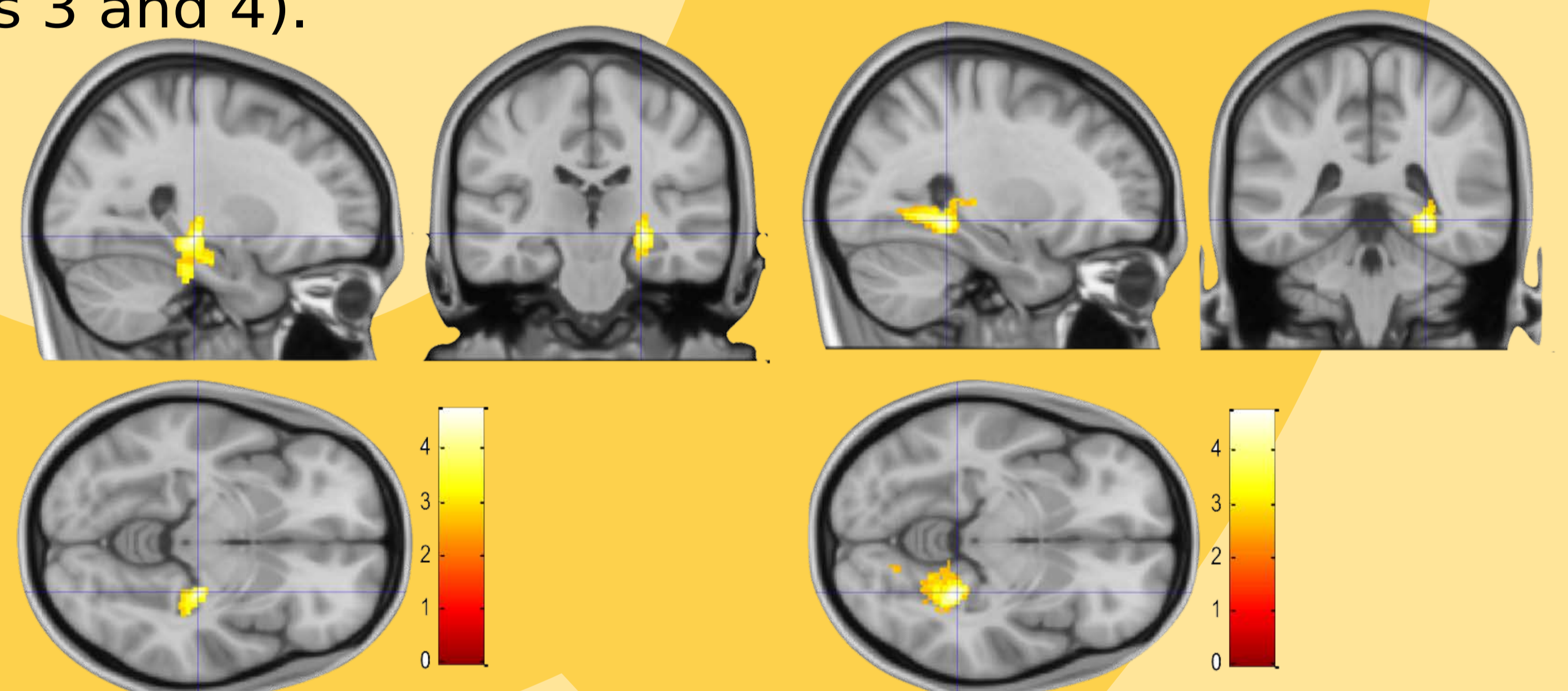


Figure 3: Multielectrode compared with conventional montage was associated with an increased connectivity between left hippocampus and left frontal pole (Alphasim corrected,  $p < 0.01$ , 469 voxels) and left superior frontal gyrus (Alphasim corrected,  $p < 0.01$ , 502 voxels).

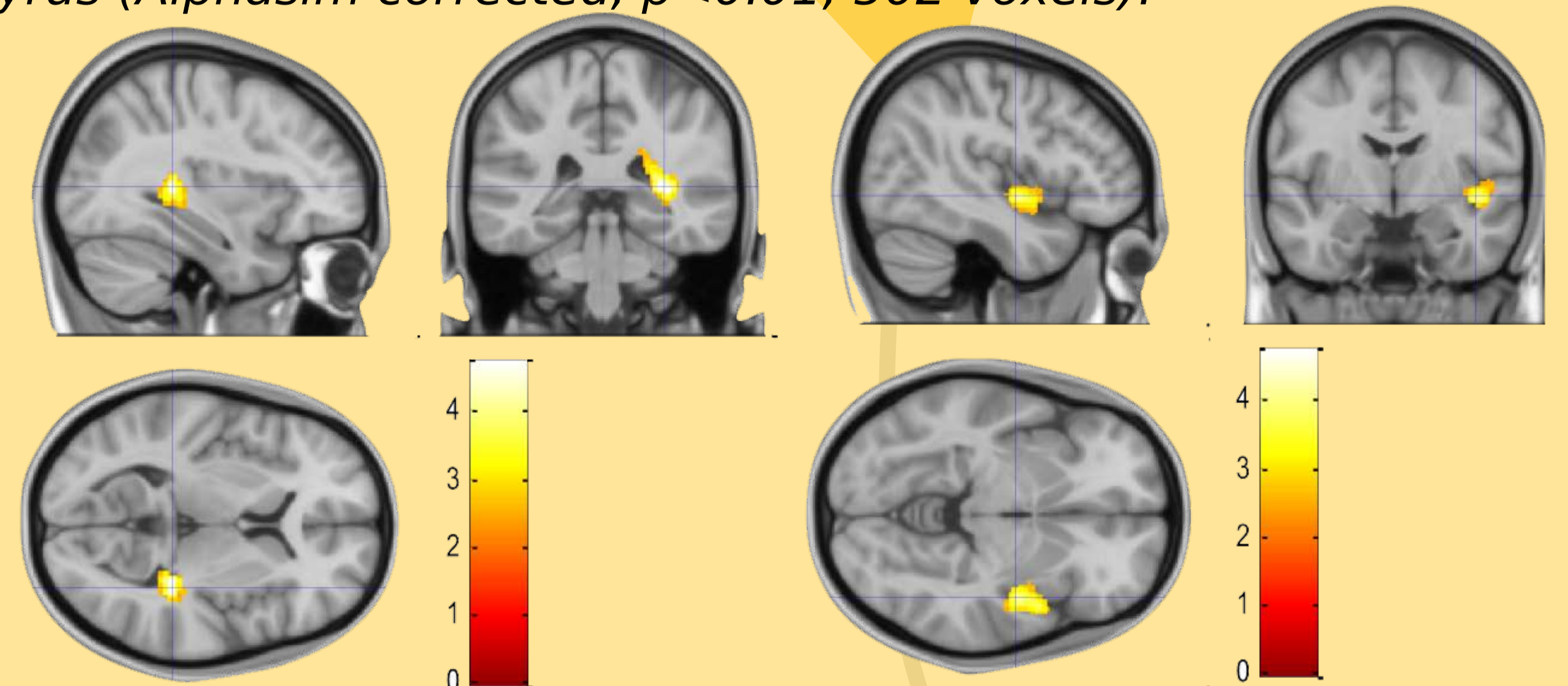


Figure 4: Multielectrode compared with conventional montage was associated with an increased connectivity between left middle frontal gyrus and left hippocampus (Alphasim corrected,  $p < 0.01$ , 483 voxels) and left anterior insula (Alphasim corrected,  $p < 0.01$ , 407 voxels).

## Conclusions

Optimized multielectrode tDCS induced a modulation on regional brain activity and FC in corticolimbic networks, thus suggesting this particular montage to be the adequate election when aiming to modulate brain activity in disorders involving corticolimbic network, which opens the possibility for new therapeutic approaches.

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